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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,529	10/16/2003	Homme W. Hellinga	GRT/1579-863	4003

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EXAMINER	
ZEMAN, ROBERT A	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
09/14/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/686,529	HELLINGA ET AL.	
	Examiner	Art Unit	
	ROBERT A. ZEMAN	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,7-15,31,32 and 38-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7-15,31,32 and 38-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed on 6-17-2011 are acknowledged. Claims 38-40 have been added. Claims 1, 2, 7-15, 31-32 and 38-40 are currently under examination.

Claim Rejections Maintained

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 7-15, 31-32 and 38-40 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,277,627 for the reasons set forth in the previous Office action in the rejection of claims 1-2, 7-15 and 31-32.

Applicant argues:

1. There is no motivation given as to why the skilled artisan would have attached one or more reporter groups at positions 10, 93 or 183.

2. There is no expectation of success shown in the Office action that attaching at least one reporter group at any position within GBP would result in the claimed biosensor.

Applicant's arguments have been fully considered and deemed non-responsive.

With regard to Point 1 since the cited patented claims encompass all possible attachment positions within the GBP and the disclosure of the cited patent contemplates the same (see column 4-5), the specific positions recited in the instant claims are deemed to be obvious variations of the patented biosensors. Moreover, the specification of U.S. Patent 6,277,627 specifically discloses that the reporter groups can be within the ligand-binding pocket (i.e. can be an endosteric site) [see column 4, lines 21-22]. Moreover, the patent's specification also discloses (via the Marvin et al. reference) the means of selecting positions for reporter groups (fluorophores) [see column 5, line 59].

With regard to Point 2, while Hellinga does not explicitly disclose the attachment of the reporter group(s) at positions 10, 93 or 183, he does disclose that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see column 4 lines 21-48). Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Hellinga attaching a reporter group, both within and outside of the binding sites (see Examples 1 and 2); the skilled artisan would have had a reasonable expectation of

success. Moreover, the patent's specification also discloses (via the Martin et al. reference) the means of selecting positions for reporter groups (fluorophores) [see column 5, line 59].

As outlined previously, although the conflicting claims are not identical, they are not patentably distinct from each other because both claims sets are drawn to biosensors comprising a bPGP and a reporter group wherein said reporter group is attached to the GBP and can constitute a fluorophore or a redox cofactor. Moreover, since the cited patented claims encompass all possible attachment positions within the GBP and the disclosure of the cited patent contemplates the same (see column 4-5), the specific positions recited in the instant claims are deemed to be obvious variations of the patented biosensors.

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-2, 7-14 and 31-32 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages

1099-1111, Friday January 5, 2001.

Applicant argues:

1. The required sequences would have been known to one of skill in the art at the time the application was filed.

2. The specification cites U.S. Patent for describing *E. coli* periplasmic binding proteins in including the amino acid sequence of glucose binding protein (GBP).

3. No specific reference to a sequence identifier is required because the GBPs are known in the art.

Applicant's arguments have been fully considered and deemed non-persuasive.

The instant claims are not limited to *E. coli* GBP. The BLAST database demonstrates that there are over 100 different GBP sequences known in the art. Consequently, the residue identifiers (which are based on the *E. coli* GBP have no correlation to a GBP for another species.

As outlined previously, the instant claims are drawn to biosensors in which at least one reporter group is attached at one or more of amino acid positions 10, 93 or 183 of a glucose binding protein

However, since no baseline sequence is provided for of the "glucose binding protein" and multiple glucose binding proteins (with differing sequences) are known in the art, none of these biosensor meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now*

claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Moreover, the skilled artisan cannot envision the detailed chemical structure of the encompassed biosensors, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

> Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404. 1405 held that:
> ...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood,* 107 F.3d at 1572, 41 USPQ2datl966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel,* 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.
>
> The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for

> rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Given that there is no disclosed correlation between the structure (sequence) of the claimed biosensor and its claimed function (an alteration in the signaling of the reporter group of said biosensor due to the binding of glucose in a glucose-binding pocket of said biosensor) the requirements of proper description have not been met.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 7-15 and 31-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection of claims 1, 7 and 8 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of term "…position 183 of said GBP..." is maintained for reasons of record.

Applicant argues:

1. The term "position" refers to the amino acid sequence of the bPBP.

2. The base sequence is the GBP amino acid sequence incorporated by reference from U.S. Patent 6,277,627.

3. No specific reference to a sequence is required because the GBPs are known in the art and numbering of their positions is known in the art.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Points 1 and 3, the instant claims are not limited to *E. coli* GBPs. Moreover, because the sequence of bPBP is variable, skilled artisan would not know what the metes and bounds of the claimed invention were. The BLAST database demonstrates that there are over 100 different GBP sequences known in the art. Consequently, the residue identifiers (which are based on the *E. coli* GBP have no correlation to a GBP for another species.

With regard to Point 2, there is no specific reference to said sequence in the rejected claim. Applicant is reminded that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

As outlined previously, given that there is no base sequence recited in the claim and there are multiple sequences for GBP known in the art at the time of filing of the instant application, it is impossible to determine what specific amino acid is being claimed.

The rejection of claim 15 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of phrase "...positions of said GBP selected from the group consisting of 10, 93 and 183." is maintained for reasons of record.

Applicant argues:

1. The term "position" refers to the amino acid sequence of the bPBP.

2. The base sequence is the GBP amino acid sequence incorporated by reference from U.S. Patent 6,277,627.

3. No specific reference to a sequence is required because the GBPs are known in the art and numbering of their positions is known in the art.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Points 1 and 3, the instant claims are not limited to *E. coli* GBPs. Moreover, because the sequence of bPBP is variable, skilled artisan would not know what the metes and bounds of the claimed invention were. The BLAST database demonstrates that there are over 100 different GBP sequences known in the art. Consequently, the residue identifiers (which are based on the *E. coli* GBP have no correlation to a GBP for another species.

With regard to Point 2, there is no specific reference to said sequence in the rejected claim. Applicant is reminded that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

As outlined previously, given that there is no base sequence recited in the claim and there are multiple sequences for GBP known in the art at the time of filing of the instant application, it is impossible to determine what specific amino acid is being claimed.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicant's statement regarding a possible declaration and request for an interview to discuss the evidence secondary factors favoring patentability of the claimed invention is noted. However, to date no declaration or secondary evidence has been made of record. Hence, any interview would be premature. Said evidence will be evaluated (and discussed with Applicant), if and when it is timely filed.

Claims 1-2, 7-15, 31-32 and 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellinga (WO 99/34212 – IDS filed 3-14-2005) for the reasons set forth in the previous Office action in the rejection of claims 1-2, 7-15 and 31-32.

Applicant argues:

1. The instant invention is directed to biosensors in which at least one reporter group is attached at one or more of amino acid positions 10, 93 or 183 of a glucose binding protein.

2. Hellinga does not teach or suggest attaching at least one reporter group to these specific positions and there is no reason provided why one of ordinary skill in the art would have attached one or more reporter groups at these specific positions.

3. The $\Delta I_{std\ or}$ ΔR_{max} values were experimentally determined by Applicant's.

4. Attaching a reporter group at amino acid position 183 provides the unexpected results of decreased binding affinity for glucose and increased fluorescence which is not taught or suggested by the art.

5. Examiner's allegation regarding the inherent properties is incorrect as these are not Section 102 rejections and the biosensors of the cited documents are not the same as the presently claimed biosensors.

6. There is not expectation of success.

7. The biosensors disclosed in the reference are different as compared to the claimed biosensors and would not have the same $\Delta I_{std\ or}$ ΔR_{max} values.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Point 2 and 4, Hellinga also discloses that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see column 4 lines 21-48). Moreover, Hellinga discloses that the binding protein can be mutated either within the binding site or at allosteric sites (see page 10, lines 14-17). While Hellinga does not explicitly disclose the attachment of the reporter group(s) at positions 10, 93 or 183, he does disclose that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see page 9, line 13 to page 10, line 14). Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Hellinga attaching a reporter group both within and outside of the binding sites (see Examples 1 and 2), the skilled artisan would have had a reasonable expectation of success.

With regard to Point 3, the mere recognition of inherent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA

1979). Thus, although the prior art does not specifically anticipate the claimed functional interactions, it is the combination of the references that would inherently lead to the modification of the immunological properties. Moreover, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

With regard to Point 4, the biosensor with a reporter group at position 183, which is encompassed by Hellinga in light of KSR, would necessarily have the same biochemical properties as that of the instant invention. Moreover, the instant claims are not limited to *E. coli* GBPs.

With regard to Point 5, In re Wiseman, 201 USPQ 658 (CCPA 1979) encompasses rejections under both Sections 102 and 103.

With regard to Point 6, Hellinga discloses that GBP is a member of a superfamily of receptor proteins and that their invention is not limited to the said "individual embodiments (see page 7, lines 11-14). Consequently, it would have been obvious to the skilled artisan to apply the teachings of Hellinga et al. to use other members of said receptor superfamily with a reasonable expectation of success.

With regard to Point 7, contrary to Applicant's assertion, the biosensors resulting from the obvious modifications of the disclosed biosensor would necessarily be the same as those of the instant claims.

As outlined previously, Hellinga discloses biosensors comprising glucose binding proteins (GBP) and reporter groups wherein said GBP include mutations that allow site-specific introduction of the environmentally sensitive reporter group (see abstract). Hellinga further discloses that said reporter groups can be site-specifically introduced by total synthesis, semi-synthesis or gene fusion (see page 7, lines 18-19) and that a variety of reporter groups can be used a fluorophores and redox cofactors (see page 8 lines 3-7 and claims 4-5). Hellinga also discloses that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see page 9, line 13 to page 10, line 14). Moreover, Hellinga discloses that the binding protein can be mutated either within the binding site or at allosteric sites (see page 10, lines 14-17).

The disclosure of Hellinga differs from the instant invention in that they don't specifically exemplify any other bPBP other than GBP. Moreover, they do not explicitly disclose the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14.

The disclosure of Hellinga differs from the instant invention in that they don't specifically exemplify the attachment of the reporter groups to positions 10, 93 or 183 of the glucose binding protein. Moreover, he does not explicitly disclose the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14.

However, Hellinga discloses that the strategy for introducing reporter groups into the exemplified GBP was successfully used with MBP and PBP. Consequently it would have been obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Hellinga attaching a reporter group both within and outside of the binding sites (see Examples 1

and 2), the skilled artisan would have had a reasonable expectation of success.

With regard to the to the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14, it is deemed in the absence of evidence to the contrary, that since the biosensors disclosed by Hellinga and those of the instant invention are the same they would necessarily have the same biochemical properties.

Claims 1-2, 7-15, 31-32 and 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellinga (U.S. Patent 6,277,627 – IDS filed 3-14-2005) for the reasons set forth in the previous Office action in the rejection of claims 1-2, 7-15 and 31-32.

Applicant argues:

1. The instant invention is directed to biosensors in which at least one reporter group is attached at one or more of amino acid positions 10, 93 or 183 of a glucose binding protein.

2. Hellinga does not teach or suggest attaching at least one reporter group to these specific positions and there is no reason provided why one of ordinary skill in the art would have attached one or more reporter groups at these specific positions.

3. The $\Delta I_{std\ or}$ ΔR_{max} values were experimentally determined by Applicant's.

4. Attaching a reporter group at amino acid position 183 provides the unexpected results of decreased binding affinity for glucose and increased fluorescence which is not taught or suggested by the art.

5. Examiner's allegation regarding the inherent properties is incorrect as these are not Section 102 rejections and the biosensors of the cited documents are not the same as the presently claimed biosensors.

6. There is not expectation of success.

7. The biosensors disclosed in the reference are different as compared to the claimed biosensors and would not have the same $\Delta I_{std\ or}$ ΔR_{max} values.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Point 2 and 4, Hellinga also discloses that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see column 4 lines 21-48). Moreover, Hellinga discloses that the binding protein can be mutated either within the binding site or at allosteric sites (see column 4, lines 49-53). While Hellinga does not explicitly disclose the attachment of the reporter group(s) at positions 10, 93 or 183, he does disclose that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see column 4 lines 21-48). Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Hellinga attaching a reporter group both within and outside of the binding sites (see Examples 1 and 2), the skilled artisan would have had a reasonable expectation of success.

With regard to Point 3, the mere recognition of inherent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Thus, although the prior art does not specifically anticipate the claimed functional interactions, it is the combination of the references that would inherently lead to the modification of the immunological properties. Moreover, the mechanism of action does not have a bearing on

the patentability of the invention if the invention was already known or obvious. Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

With regard to Point 4, the biosensor with a reporter group at position 183, which is encompassed by Hellinga in light of KSR, would necessarily have the same biochemical properties as that of the instant invention. Moreover, with regards to Applicant's reference to a possible declaration, said declaration will be evaluated when and if it is timely filed.

With regard to Point 5, In re Wiseman, 201 USPQ 658 (CCPA 1979) encompasses rejections under both Sections 102 and 103.

With regard to Point 6, Hellinga discloses that GBP is a member of a superfamily of receptor proteins and that their invention is not limited to the said "individual embodiments (see page 7, lines 11-14). Consequently, it would have been obvious to the skilled artisan to apply the teachings of Hellinga et al. to use other members of said receptor superfamily with a reasonable expectation of success. Moreover, the reference's specification also discloses (via the Marvin et al. reference) the means of selecting positions for reporter groups (fluorophores) [see column 5, line 59].

With regard to Point 7, contrary to Applicant's assertion, the biosensors resulting from the obvious modifications of the disclosed biosensor would necessarily be the same as those of the instant claims.

As outlined previously, Hellinga discloses biosensors comprising glucose binding proteins (GBP) and reporter groups wherein GBP said include mutations that allow site-specific introduction of the environmentally sensitive reporter group (see abstract). Hellinga further discloses that said reporter groups can be site-specifically introduced by total synthesis, semi-synthesis or gene fusion (see column 1, lines 46-48) and that a variety of reporter groups can be used a fluorophores and redox cofactors (see column 3, lines 48-52 and claims 4-5). Hellinga also discloses that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see column 4 lines 21-48). Moreover, Hellinga discloses that the binding protein can be mutated either within the binding site or at allosteric sites (see column 4, lines 49-53).

The disclosure of Hellinga differs from the instant invention in that they don't specifically exemplify the attachment of the reporter groups to positions 10, 93 or 183 of the glucose binding protein. Moreover, he does not explicitly disclose the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14.

However, Hellinga discloses that the strategy for introducing reporter groups into the exemplified GBP was successfully used with MBP and PBP. Consequently it would have been obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Hellinga attaching a reporter group both within and outside of the binding sites (see Examples 1 and 2), the skilled artisan would have had a reasonable expectation of success.

With regard to the to the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14, it is deemed in the absence of evidence to the contrary, that since the biosensors disclosed by

Hellinga and those of the instant invention are the same they would necessarily have the same biochemical properties.

Claims 1-2, 7-15 and 38-40 under 35 U.S.C. 103(a) as being unpatentable over Amiss et al. (US 2003/0134346) for the reasons set forth in the previous Office action in the rejection of claims 1-2 and 7-15.

Applicant argues:

1. The instant invention is directed to biosensors in which at least one reporter group is attached at one or more of amino acid positions 10, 93 or 183 of a glucose binding protein.

2. Hellinga does not teach or suggest attaching at least one reporter group to these specific positions and there is no reason provided why one of ordinary skill in the art would have attached one or more reporter groups at these specific positions.

3. The $\Delta I_{std\ or}$ ΔR_{max} values were experimentally determined by Applicant's.

4. Attaching a reporter group at amino acid position 183 provides the unexpected results of decreased binding affinity for glucose and increased fluorescence which is not taught or suggested by the art.

5. Examiner's allegation regarding the inherent properties is incorrect as these are not Section 102 rejections and the biosensors of the cited documents are not the same as the presently claimed biosensors.

6. There is not expectation of success.

7. The biosensors disclosed in the reference are different as compared to the claimed biosensors and would not have the same $\Delta I_{std\ or}$ ΔR_{max} values.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Point 2 and 4, Amiss et al. disclose biosensors comprising galactose/glucose binding proteins (GGBP) and reporter groups wherein said GGBP includes at least on mutation and at least one reporter group (paragraph 0017). Amiss further discloses does disclose that said reporter groups can be attached covalently to cysteine residues. Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]).

With regard to Point 3, the mere recognition of inherent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Thus, although the prior art does not specifically anticipate the claimed functional interactions, it is the combination of the references that would inherently lead to the modification of the immunological properties. Moreover, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

With regard to Point 4, the biosensor with a reporter group at position 183, which is encompassed by Amiss et al. in light of KSR, would necessarily have the same biochemical properties as that of the instant invention.

With regard to Point 5, In re Wiseman, *201* USPQ 658 (CCPA 1979) encompasses rejections under both Sections 102 and 103.

With regard to Point 6, given the success of Amiss attaching a reporter group to positions 11, 14, 19, 43, 74, 07, 110, 110, 112, 113, 137, 149, 152, 153, 213, 216, 238, 287 and 292, the skilled artisan would have had a reasonable expectation of success. Moreover, the reference's specification also discloses (via U.S. Patent 6,277,627 and the Marvin et al. reference) the means of selecting positions for reporter groups (fluorophores) [see paragraph [0009]].

With regard to Point 7, contrary to Applicant's assertion, the biosensors resulting from the obvious modifications of the disclosed biosensor would necessarily be the same as those of the instant claims.

As outlined previously, Amiss et al. disclose biosensors comprising galactose/glucose binding proteins (GGBP) and reporter groups wherein said GGBP includes at least on mutation and at least one reporter group (paragraph 0017). Amiss et al. further disclose that mutations of binding proteins include the addition or substitution of cysteine groups, non-naturally occurring amino acids and replacement of substantially non-reactive amino acids with reactive amino acids to provide for the covalent attachment of electrochemical or photoresponsive reporter groups (see paragraph 0025) and that a variety of reporter groups can be used such as fluorophores (e.g. acrylodan - see paragraph [0031]) and redox cofactors (see paragraph [0032]). Amiss et al. also disclose that said reporter groups can be attached to the GGBPs by any conventional means throughout the length of the protein. (see paragraph 0034). It should be noted that while Amiss et al. do not explicitly disclose the attachment of the reporter group(s) at positions 10, 93 or 183, Amiss does disclose that said reporter groups can be attached covalently to cysteine residues.

Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Amiss attaching a reporter group to positions 11, 14, 19, 43, 74, 07, 110, 110, 112, 113, 137, 149, 152, 153, 213, 216, 238, 287 and 292, the skilled artisan would have had a reasonable expectation of success.

With regard to the to the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14, it is deemed in the absence of evidence to the contrary, that since the biosensors disclosed by Amiss et al. are and those of the instant invention are the same they would necessarily have the same biochemical properties.

Claims 1-2, 7-15 and 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amiss et al. (US Patent 6,855,556) for the reasons set forth in the rejection of claims 1-2 and 7-15.

Applicant argues:

1. The instant invention is directed to biosensors in which at least one reporter group is attached at one or more of amino acid positions 10, 93 or 183 of a glucose binding protein.

2. Hellinga does not teach or suggest attaching at least one reporter group to these specific positions and there is no reason provided why one of ordinary skill in the art would have attached one or more reporter groups at these specific positions.

3. The $\Delta I_{std\ or}$ ΔR_{max} values were experimentally determined by Applicant's.

4. Attaching a reporter group at amino acid position 183 provides the unexpected results of decreased binding affinity for glucose and increased fluorescence which is not taught or suggested by the art.

5. Examiner's allegation regarding the inherent properties is incorrect as these are not Section 102 rejections and the biosensors of the cited documents are not the same as the presently claimed biosensors.

6. There is not expectation of success.

7. The biosensors disclosed in the reference are different as compared to the claimed biosensors and would not have the same $\Delta I_{std\ or}$ ΔR_{max} values.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Point 2 and 4, Amiss et al. disclose biosensors comprising galactose/glucose binding proteins (GGBP) and reporter groups wherein said GGBP includes at least on mutation and at least one reporter group (paragraph 0017). Amiss further discloses does disclose that said reporter groups can be attached covalently to cysteine residues. Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]).

With regard to Point 3, the mere recognition of inherent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Thus, although the prior art does not specifically anticipate the claimed functional interactions, it is the combination of the references that would inherently lead to the modification

of the immunological properties. Moreover, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

With regard to Point 4, the biosensor with a reporter group at position 183, which is encompassed by Amiss et al. in light of KSR, would necessarily have the same biochemical properties as that of the instant invention. Moreover, with regards to Applicant's reference to a possible declaration, said declaration will be evaluated when and if it is timely filed.

With regard to Point 5, In re Wiseman, *201* USPQ 658 (CCPA 1979) encompasses rejections under both Sections 102 and 103.

With regard to Point 6, given the success of Amiss attaching a reporter group to positions 11, 14, 19, 43, 74, 07, 110, 110, 112, 113, 137, 149, 152, 153, 213, 216, 238, 287 and 292, the skilled artisan would have had a reasonable expectation of success. Moreover, the reference's specification also discloses (via U.S. Patent 6,277,627 and the Marvin et al. reference) the means of selecting positions for reporter groups (fluorophores) [see title page and column 2, lines 14-26].

With regard to Point 7, contrary to Applicant's assertion, the biosensors resulting from the obvious modifications of the disclosed biosensor would necessarily be the same as those of the instant claims.

As outlined previously, Amiss et al. disclose biosensors comprising galactose/glucose binding proteins (GGBP) and reporter groups wherein said GGBP includes at least on mutation and at least one reporter group (column 3, lines 44-50). Amiss et al. further disclose that mutations of binding proteins include the addition or substitution of cysteine groups, non-naturally occurring amino acids and replacement of substantially non-reactive amino acids with reactive amino acids to provide for the covalent attachment of electrochemical or photoresponsive reporter groups (see column 5, lines 1-7) and that a variety of reporter groups can be used such as and redox cofactors (see column 6, lines 55-59). Amiss et al. also disclose that said reporter groups can be attached to the GGBPs by any conventional means throughout the length of the protein (see column 6 line 65 to column 7, line 8). It should be noted that while Amiss et al. do not explicitly disclose the attachment of the reporter group(s) at positions 10, 93 or 183, Amiss does disclose that said reporter groups can be attached covalently to cysteine residues. Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Amiss attaching a reporter group to positions 11, 14, 19, 43, 74, 07, 110, 110, 112, 113, 137, 149, 152, 153, 213, 216, 238, 287 and 292, the skilled artisan would have had a reasonable expectation of success.

With regard to the to the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14, it is deemed in the absence of evidence to the contrary, that since the biosensors disclosed by Amiss et al. are and those of the instant invention are the same they would necessarily have the same biochemical properties.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT A. ZEMAN whose telephone number is (571)272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m. .

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Patricia Duffy can be reached on (571) 272-0855. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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/Robert A. Zeman/
Primary Examiner, Art Unit 1645
September 12, 2011